Evaluation of Late Onset Bipolar Illness During Menopause

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Abstract

Objective: *The purpose of this paper is to review the literature on bipolar illness and to discuss its relevance to the evaluation and treatment of bipolar illness during menopause. The hypothesis is that there is a group of patients who may present with commonly reported symptoms of menopause who are in fact, suffering from an underlying bipolar illness.*

Method: *The literature pertaining to gender differences in bipolar illness as well as the effect of major life events associated with the onset of bipolar illness is closely examined.*

Results: *There is enough evidence to support the hypothesis that women in particular are vulnerable to bipolar illness of the rapid cycling type. Exacerbations of a previous existing condition or late-onset bipolar illness may be associated with major stressors and life events such as that experienced during menopause.*

Conclusions: *Gender differences in the course of bipolar illness and the greater prevalence of rapid cycling among bipolar women may in fact be a major consideration in the evaluation and treatment of symptoms during menopause.*

Introduction

Although gender differences in the evaluation and treatment of bipolar illness have been recognized, the impact of this illness on the experience of menopause is a topic that has yet to be explored. Commonly reported symptoms of menopause including irritability, sleep disturbances, and mood changes may in fact, be complicated or worsened by an underlying bipolar disorder. Another consideration is the possibility that there are women who are suffering from the first episode of a late onset bipolar illness. In light of the fact that 40% of the U.S. population is expected to be 45 years and older by the year 2010, this appears to be an area of research that warrants further examination for its clinical relevance.[1]

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Table 1.– Type I bipolar disorder (history of at least one manic episode)
From DSM-IV, American Psychiatric Association, 1994 p.332 (29)

-Criteria for manic episode:

-Distinct period of abnormally and persistently elevated, expansive, or irritable mood, lasting at least 1 week (can be less than 1 week if hospitalization required).

-At least three of the following symptoms (four if mood can only be described as irritable):

Grandiosity
Decreased need for sleep
Pressure of speech or more talkative than usual
Racing thoughts or flight of ideas
Highly distractable
Psychomotor agitation or increase in goal-directed activity
Excessive involvement in pleasurable activities with a high potential for painful consequences

-Mood disturbance severe enough to cause marked impairment in social or occupational functioning. Psychotic features may also be included in this category.

Table 2.– Type II bipolar disorder (recurrent major depressive episodes with hypomanic episodes)
From DSM-IV, American Psychiatric Association, 1994 p.338 (29)

Criteria for hypomania:

-A distinct period of persistently elevated, expansive, or irritable mood lasting at least 4 days.

-During the period of mood disturbance, at least three (four if the mood is only irritable) symptoms of mania have been present to a significant degree.

-The episode is not severe enough to cause a marked impairment in social or occupational functioning. No psychotic features. Hospitalization not necessary to keep the patient safe from self or others.

Review of literature

According to the literature the median age of onset of bipolar disorder in women living in the United States is 34.5 years.[2] The peak incidences, however, occur at ages 20-30 and 40-50 years. The latter peak clearly coincides with the age at which most women in the United States are in menopause. Leibenluft suggests that women may be more likely to experience the onset of bipolar illness at ages 45-49 years.[3]

Currently, the Diagnostic and Statistical Manual of Mental Disorders DSM-IV acknowledges the existence of various subtypes of bipolar illness. The description of the classic type I manic-depressive is the one with which most clinicians are familiar (Table 1). The type II bipolar patient, on the other hand, may present with more subtle clinical features, as they do not present with full blown manic symptoms, but rather attenuated symptoms that are described as hypomania (Table 2). Unfortunately, this latter group can be difficult to identify and to treat, thus often becoming labeled as having borderline personality traits. Symptoms that may lend themselves to this diagnosis include rapid shifts in mood that are attributed to affective instability, intense displays of anger or irritability, impulsivity, recurrent threats of self harm or suicide, and major disruptions in interpersonal relationships.

Bipolar illness can be further classified according to the frequency with which the episodes of depression are intercalated with mania or hypomania. A rapid cycling bipolar illness is defined as the presence of at least four episodes of a mood disturbance in the previous 12 months that meet the criteria for a major depressive, manic, mixed, or hypomanic episode. A mixed episode refers to a mood disturbance that meets the criteria for both a manic episode and a major depressive episode.

Most of the research on gender differences in bipolar illness has focused upon reproductive factors associated with pregnancy and the postpartum period. Out of two studies that included menopause as part of the evaluation of bipolar illness, one group of authors, Kukopulos et al.[4] found that about a third of the bipolar women in their study became what was described as "continuous circular" bipolars around the period of menopause. Wehr et al.,[5] however, noted no effect of menopause in bipolar patients who had already been identified as rapid cyclers. What remains to be explored is whether there is a group of women who experience the first episode of a late onset bipolar illness during menopause.

In making an assessment of the factors that lend themselves to the etiology of a late onset bipolar illness, it becomes clear that genetic and biological components alone are not adequate in explaining the heterogeneity observed in the expression of this disorder. In one study conducted by Ellicott et al.[6] it was found that there is a significant association between life events and the relapse or recurrence of bipolar illness. Not only was it reported that bipolar individuals experience increased stress before the onset of their illness, but also prior to subsequent episodes. In another study, Glassner et al.[7] observed that life events appear to play a greater etiological role in late onset bipolar disorder. A treatment plan that attempts to identify and ameliorate potential life stressors may be very important in reducing the likelihood of relapse in bipolar patients. In some cases, it may even prevent or at least delay the onset of bipolar illness during the perimenopausal years.

Although some may argue that menopause is not necessarily experienced by all women as a stressful live event, it is important to keep in mind that the women who present for the treatment of menopausal symptoms are usually in a measurable amount of distress. As of yet, a clear cut syndrome of an affective disorder associated with menopause has not been identified with consistency. However, there appears to be a general consensus in the literature documenting an increase in somatic, mood, and behavioral symptoms.[8] Studies have shown that women in menopause clinics are reported to have elevated symptoms of depression and a reduced quality of life.[9] According to Harlow et al.,[10] there may actually be a link to medically treated depression and early menopause. This in itself can be an important consideration in the primary care setting where clinicians can initiate appropriate intervention strategies early in the course of a woman's reproductive history.

Differential diagnosis

Assessing older patients for bipolar illness can present with some difficulties that complicate the clinical picture. Unlike the classic presentation of an agitated, full-blown manic patient with pressure of speech and grandiose delusions, older patients are more likely to present with signs of a mixed episode in which symptoms of both depression and mania are present.[11] In a study by Schulman et al.[12] it was reported that less than 10% of a group of elderly bipolar patients were found to have had their first manic attack before the age of 40. Without a thorough diagnostic evaluation, many older patients may be incorrectly diagnosed as having an agitated depression, a schizoaffective disorder, or borderline personality traits with somatic preoccupation. The danger in this is that these patients may be at increased risk for rapid cycling and worsening of irritability, especially if antidepressant therapy is initiated without a mood stabilizer.[13]

Considering the statistics that indicate that rapid cycling bipolar disorder is three times more common in women than in men,[14] the issue of appropriate mood stabilization and follow-up treatment becomes even more critical in the primary care setting. Not only are these women more likely to present themselves initially to internists and gynecologists during the reproductive years, but also, the likelihood in the recurrence of symptoms in subsequent years is well documented.[3,15]

Clinical course

In order to carefully assess the clinical presentation with accuracy, one must always obtain a detailed history and a description of the clinical course of the menopausal woman's symptoms. Signs and symptoms associated with menopause tend to develop insidiously and are believed to be linked to a gradual decline in hormone activity. Mood disturbances and irritability that last for at least a week and continue to escalate are suggestive of an affective disorder rather than a worsening of severe menopausal symptoms. A thorough medical work-up to exclude general medical conditions such as thyroid abnormalities can be especially helpful. Several studies in the literature have demonstrated that rapid cycling patients can be successfully treated with high doses of levothyroxine.[16,17] Other considerations in the differential diagnosis also include substance abuse and drug interactions, especially if a woman is on oral contraceptives, hormone replacement therapy, or antidepressants that can alter the pharmacokinetics of drug metabolism.[18]

Facilitation of diagnosis

Sleep disturbances are common during menopause.[19] Hot flashes which are believed to be a symptom of vasomotor instability are especially disruptive to the sleep cycle. Not only does a lack of sleep cause fatigue, but it also has a profound effect on mood, memory, and concentration as measured by cognitive performance tasks, probed memory examinations, and electrodermal-orienting responses

to assess attentional shift or capture.[20,21,22] Sleep deprivation in itself has been known to trigger manic episodes in some bipolar patients.[23] The psychological ramifications of hot flashes has also been noted by Ginsberg[24] and Baker et al.[25] in the literature. Once again, a detailed history will reveal clues as to whether there is an underlying mood disorder, or whether it is a symptom that might be ameliorated by hormone replacement therapy.

A patient who reports a sudden decrease in sleep along with an increase in goal-directed activity and irritability is more likely to be suffering from a bipolar disorder than a woman who finds herself feeling constantly fatigued and low in energy because of sleep disturbances related to hot flashes. The difficulty arises, however, when bipolar patients with mixed features present with a combination of symptoms that include lack of sleep, irritability, fatigue, and possibly an increase in goal-directed activities. At this point, it becomes especially critical to evaluate the patient for other supporting evidence such as racing thoughts, grandiosity, excessive involvement in pleasurable activities with a high potential for painful consequences, significant changes in weight, or suicidal ideation, none of which are considered to be a normal part of menopause. When there is a suspicion that an underlying psychiatric illness is present, it is important to ask the patients directly about these symptoms as they usually will not volunteer this information on a routine visit to their primary health care provider.

Treatment

Pharmacological intervention continues to be the mainstay of treatment for bipolar illness. For this reason, an accurate diagnosis and initiation of treatment is critical. In contrast to earlier reports that had suggested that perhaps interruptions in lithium maintenance therapy could lead to a refractory response in previously treated patients,[26] Tondo et al.[27] has shown that in fact, lithium treatment can successfully be restarted if there is a prior history of a positive response. Of particular concern are the cases of bipolar illness that are untreated. Not only can the illness recur more frequently, but it is also known to progress rapidly over time. A phenomenon known as the kindling hypothesis of affective disorders suggests that perhaps with repeated episodes of illness, it may be possible that subsequent episodes increase in frequency and intensity. A study by Cutler et al.[28] revealed that untreated patients with severe symptoms of bipolar illness had a tendency to have more rapid recurrences as the history of the illness progressed.

Conclusions

The evidence in the literature suggests that gender differences in the course of bipolar illness and the greater prevalence of rapid cycling among bipolar women may in fact be a major consideration in the evaluation and treatment of commonly related symptoms during menopause. Although most women undergoing menopause are not likely to be suffering from a major affective disorder requiring intensive psychiatric treatment, those who may have a subclinical psychiatric illness or have a genetic vulnerability to experience a reproductively related affective disorder may find that menopause is the first time that their psychiatric condition is recognized. This could be partly due to a combination of psychosocial stressors that make themselves apparent during the time of menopause, but also, to biological factors such as decreased sleep that may trigger the onset of a bipolar illness in susceptible individuals. An accurate diagnosis not only ensures the implementation of an appropriate treatment plan for the patient, but it is also the quickest and most cost-efficient mechanism by which we can alleviate the suffering for which we, as medical health providers, are called upon.

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